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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,506	12/20/2001	Herve Jean-Clement Coste	PF3623USW	6111

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EXAMINER	
VOGEL, NANCY S	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 02/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/936,506	COSTE ET AL.	
	Examiner	Art Unit	
	Nancy Vogel	1636	

-- The MAILING DATE of this communication appears on th cover sheet with th correspond nc addr ss --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *18-26 and 32-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 and 27-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 September 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/11/01 & 11/17/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-34 are pending in the case. Receipt of the response to the requirement for restriction/election on 12/22/03 is acknowledged.

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-17, and 27-31 in the paper submitted 12/22/03 is acknowledged.

Claims 18-26, and 32-34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. submitted 12/22/03.

Specification

The disclosure is objected to because of the following informalities:.

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See page 5 of the specification. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Although claims 9-17 and 27 directly or indirectly depend on claim 1, they include the possibility of DNA molecules other than the 5'UTR of the human hsp70 gene being present, due to the use of the term "comprising" . The vector of claim 9, for instance, "comprises" a DNA molecule according to claim 1, but may also "comprise" any other DNA molecule such as the human hsp70 promoter and/or gene. The same applies to the expression systems of claims 10-15, the method using the expression system of claim 10 , as recited in claim 16 and by dependence claim 17, and the use of the vectors "comprising" the sequence of claim 1, as recited in claim 27.

Claims 9-11, 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Hunt et al. (Proc. Natl. Acad. Sci. 82: 6455-6459, 1985) (cited by applicants).

Hunt et al. disclose recombinant DNA molecules comprising the 5' untranslated region of a human hsp70 clone (see page 6455, second column, 1st paragraph, lines 1-4 of Materials and Methods; Fig. 2). The human hsp70 gene including the 5' untranslated region, is present in a phage vector, present in a cell.

Claims 9-17 and 27 are rejection under 35 U.S.C. 102(b) as being anticipated by Bromley et al. (WO87/00861) (cited by applicants).

Bromley et al. disclose a plasmid expression vector comprising the human hsp70 5'untranslated leader sequence fused to the hGH coding region (page 10, second complete paragraph). The reference discloses eukaryotic cells comprising the expression vector (page 10, third complete paragraph).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The following factors have been considered in formulating this rejection (*In re Wands*, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance

presented, the presence or absence of working examples of the invention, and the quantity of experimentation necessary.

The present claims are very broad. Claims 28-31 encompass DNA molecules of claim 1 that can be used in any type of therapy, including any type of therapeutic or prophylactic vaccination.

The nature of the invention is DNA molecules to be useful as therapy, or treatment of disease. The delivery of a nucleic acid in vivo or ex vivo for therapeutic reasons constitutes gene therapy.

An analysis of the prior art as of the effective filing date of the present application shows the complete lack of documented success for any treatment based on gene therapy. In a review on the current status of gene therapy, both Verma et al (Nature (1997) 389:239-242) and Palu et al. (J. Biotechnol. (1999) 68:1-13) state that despite hundreds of clinical trials underway, no successful outcome has been achieved. See Verma et al. p. 239, 1st paragraph; Palu et al., p. 1, Abstract. The continued, major obstacles to successful gene therapy are gene delivery and sustained expression of the gene. While both references indicate the promise of gene therapy, it is still a technique of the future and advancements in our understanding of the basics of gene delivery and expression must be made before gene therapy becomes a useful technique. See Verma et al. p. 242, col. 2-3; and Palu et al, pp. 10-11.

The relative skill of those in the art of stem cell culture and recombinant DNA technology is high.

The area of the invention is unpredictable. As discussed above, the method of in vivo or ex vivo gene therapy is highly complex and unpredictable. Indeed, the recent tragic and unexpected death of a participant in a gene therapy clinical trial clearly illustrates the unpredictable nature of gene therapy. See Fox, ASM News, Feb. 2000, 66 (2):1-3. More recently, two children treated with retroviral gene therapy for SCID have been diagnosed with leukemia, further indication of the unpredictable nature of gene therapy which persists to the present time. See Fox, Yahoo! News, January 14, 2003, cited by the examiner. The skilled artisan at the time the present invention was made recognized the difficulty of achieving sufficient heterologous gene expression to induce any therapeutic effect.

The present specification provides little or no guidance to support the claimed invention for gene therapy applications. The specification discloses methods of administration and formulations of the disclosed DNA molecules which may be utilized for treating diseases (pages 8- 12). There is no direction provided as to how to overcome the obstacles to gene therapy recognized by leaders in the field, i.e. transient gene expression, difficulties in targeting specific cells, unpredictability of integration site or localization of the administered DNA in the target cell, etc.

The working examples disclosed directed toward in vivo treatment consist of one experiment of immunization using a plasmid containing the hsp70 5' untranslated region linked to a gene.

The quantity of experimentation necessary to carry out the claimed invention is high as the skilled artisan could not rely on the prior art or the present specification to

teach how to use the claimed methods. In order to determine how to use the method of gene therapy to treat a condition, one of skill in the art would have to determine amounts and timing of administration, method and location of administration, levels of expression needed for effective treatment, etc. Since neither the prior art nor the specification provides the answers to all of these questions, it would require a large quantity of trial and error experimentation by the skilled artisan to do so.

Based on the broad scope of the claims, the unpredictability in the area of the invention, the lack of sufficient guidance or working examples in the specification and the quantity of the experimentation necessary, it would clearly require undue experimentation by one of skill in the art to determine how to make and/or use the claimed methods of treatment using the disclosed DNA molecules and expression systems.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-17 and 27-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, and by dependence, claims 2-17, and 27-31, are vague and indefinite in the failure to recite the location of the recited DNA molecule in respect to the recited region encoding a polypeptide. Although the claim recites that said DNA is operably linked to said region encoding a polypeptide, presumably it is intended that the DNA is

operably linked to the 5' end of said region. The claims have been examined as if this was recited.

Claim 27 provides for the use of the DNA of claim 1, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 27 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 6:30 - 3:00, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ntv

JAMES KETTER
PRIMARY EXAMINER